Remarks

Priority:

The claims of priority to 13.04 has been denied for lack of literal support for the term siRNA in the priority document. An siRNA is a double stranded oligonucleotide that causes inhibition of expression of a gene. Support for delivery of an oligonucleotide via intravascular injection is provided in the priority document at column 3 lines 23-26. Support for RNA is provided in the priority document at column 6 lines 18-20. That the RNA may be double stranded RNA is provided in the priority document at column 6 lines 35-36. That a polynucleotide may be delivered to cause inhibition of gene expression is provided in the specification at column 6 lines 40-43. Therefore, support for siRNA is inherently supported in the specification of the priority document.

Objection to the claims:

Claims17 and 18 have been amended as recommended by the Examiner to obviate the objections. A period has been placed at the end of claim 17 and "claim" has been spelled correctly in claim 18.

Double Patenting:

Claims 11-17 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 16-19 of copending Application No. 10/012,804. With this response, Applicants have filed a terminal disclaimer to overcome the rejection.

Claims 11-17 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 3-8 and 11-14 of U.S. Patent No. 6,379,966. With this response, Applicants have filed a terminal disclaimer to overcome the rejection.

Rejection of the claims under 35 USC §103

Claims 11-18 have been rejected under 35 U.S. C. 103 as being unpatentable over Zimmer (Methods, 1999) in view of Elbashir et al (Nature 2001) and Zhang et al (Human Gene Therapy 1999). The action states that Zimmer taught injecting antisense oligonucleotides complexed with positive and negative polymers into the tail vein of mice and observing delivery to the liver. Applicants respectfully disagree. In describing tail vein injection of oligonucleotides, Zimmer et al. refer to two publications: Nakada et al. (1996) and Fattall et al. (1998) (attached). Neither Zimmer, Nakada, nor Fattal describe any functional activity of the oligonucleotides in the liver following tail vein injection. Functional delivery in vivo, as taught by Zimmer, is limited to subcutaneous injection into an implanted tumor (see the first full paragraph on page 293). It is well known in the art that many different compounds, when injected into the blood stream, are taken up by the liver for degradation and removal. Therefore, showing mere accumulation in the liver, is insufficient to demonstrate functional delivery to the liver. As demonstrated in the examples, Applicants have shown functional delivery of siRNA to cells in vivo as evidenced by the sequence-specific inhibition of gene expression.

The action states that any injection into the tail vein is equivalent to increasing vessel permeability because the injection itself would inherently increase pressure in the area of injection at the time of injection. Applicants have amended Claim 1 to be more specific. Claim 1 now indicates "increasing the permeability of vessels within the target tissue." This amendment incorporates the limitation of claim 2 into claim 1. This is in contrast to the data referenced by Zimmer where the pressure is limited to the point of the tail vein injection.

Because Zimmer et al. did not teach functional delivery of oligonucleotides complexes to cells in vivo by injection into a vessel, it would not have been obvious to combine the teachings of Elbashir or Zhang with the teachings of Zimmer. Applicants respectfully request reconsideration of this 103 rejection.

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Amdt. dated Oct. 24, 2005
Reply to Office action of Aug. 24, 2005

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 11-18 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as express mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this date: 10/24/2005

Kirk Ekena

[REPLACEMENT SHEET]

This Patent Application is related to pending United States patent applications 60/315,394 filed August 27, 2001, 60/324,155 filed September 20, 2001 and 09/450,315, now US Patent 6,379,966, filed November 29, 1999.